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| APPLICATION NO.                                     | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.           | CONFIRMATION NO. |
|---|-------------|----------------------|-------------------------------|------------------|
| 10/616,477  | 07/09/2003  | Michael A. Zeligs    | 9439-015                      | 9606             |
| 20583   | 7590        | 06/29/2007           |                               |                  |
| JONES DAY<br>222 EAST 41ST ST<br>NEW YORK, NY 10017 |             |                      | EXAMINER<br>EBRAHIM, NABILA G |                  |
|   |             |                      | ART UNIT                      | PAPER NUMBER     |
|   |             |                      | 1618                          |                  |
|   |             |                      | MAIL DATE                     | DELIVERY MODE    |
|   |             |                      | 06/29/2007                    | PAPER            |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |  |  |
|------------------------------|--------------------------------------|--|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/616,477 | <b>Applicant(s)</b><br>ZELIGS, MICHAEL |  |
|                              | <b>Examiner</b><br>Nabila G. Ebrahim | <b>Art Unit</b><br>1618                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>4/18/07</u> . | 6) <input type="checkbox"/> Other: ____  |

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### **DETAILED ACTION**

Receipt of the Information Disclosure Statement, Applicant's remarks and amendments to the claims dated 4/18/07 is acknowledged.

#### ***Status of Claims***

Claims 1-7, and 15 are pending in the application.

Claims 8-14 were cancelled.

Claim 15 is new.

***Status of Office Action:*** Final

#### ***Information Disclosure Statement***

1. The information disclosure statement filed 4/18/07 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

#### ***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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2. Claim 1, 2, 7, and 15 remain rejected under 35 U.S.C. 102(a) as being anticipated by Liang Jin et al (Liang, j. et al. *cancer research* 1999, 59, 3991-3997), hereinafter "Liang" for the reasons set forth in the office action dated 8/25/06.

Regarding new claim 15 which specifies the use of the indole compounds for human females, it is deemed inherent that Liang used female animals as an animal model to conclude results for treating human females. This is evidenced by the disclosure of Liang that dietary I3C functions as a potent inducer of 2-hydroxylation of estradiol in rodents and humans, thus increasing the antiproliferative metabolite 2-hydroxyestrone and decreasing 16 $\alpha$ -hydroxyestrone. This change in estrogen metabolism may be the reason, at least in part, why I3C inhibits mammary tumorigenesis in various mouse models (see introduction).

### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-7, and 15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Liang Jin et al (Liang, j. et al. *cancer research* 1999, 59, 3991-3997), hereinafter "Liang" in view of Firestone et al. US 6001868 "Firestone", and further in view of Kunz et al. US 5981568 "Kunz" for the reasons set forth in the office action dated 8/25/06.

***Response to Arguments***

4. Applicant's arguments filed 4/18/07 have been fully considered but they are not persuasive.

Applicant contends that Liang does not disclose the treatment of cervical dysplasia, either expressly or inherently. Liang only discloses the prevention of cervical-vaginal cancer or cervical dysplasia. There is nothing in Liang that would indicate that I3C would be useful for treatment of vaginal cancer or cervical dysplasia. Applicant also argues that Liang does not disclose the treatment of cervical dysplasia by administering DIM, either expressly or inherently. The only disclosure in Liang with respect to DIM is in page 3997, col. 1, lines 18-19. Liang merely discloses that I3C and one of its condensation products, i.e., DIM are available as supplement.

This was not found persuasive because Liang teaches that the study indicates that I3C acts as a chemopreventive for cervicalvaginal cancer and other papillomavirus disease. The research' results also indicate that I3C would not only prevent cervical cancer but also reduce cervical hyperplasia and dysplasia (see page 3997, last paragraph). Liang's disclosure of DIM stating that "I3C and one of its condensation products, i.e, DIM are available as supplement" is sufficient to show that both compounds are equivalent to treat the condition (this is known in the art as evidenced by patent US 6399645, the reference is provided by the Applicant in the IDS dated 4/18/07).

Applicant argues that Liang does not teach any specific use of DIM. The disclosure is preceded by the words "...condensation of I3C into its active derivatives depends on acids in the stomach (38, 39)." This sentence clearly teaches that there are

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many derivatives (plural) of I3C. The paragraph as a whole does not teach that DIM is an active derivative of I3C, nor that any single reaction product from I3C would be sufficient to prevent cervical dysplasia.

This was not found persuasive because, Liang teaches literally that I3C and its acid condensation product diindolymethane (DIM) are available as supplements, which show equivalency of the use of the compound and its derivative and also the equivalency of the effects expected from the two compounds.

Applicant argues that Firestone does not remedy the deficiencies of Liang, Firestone does not teach treatment of cervical dysplasia nor does Firestone teach that DIM would be useful for the treatment of cervical dysplasia.

To respond to this argument, it is noted that Firestone was introduced to the rejection to show that at the time the invention was made it was known that phytochemicals were used in different dosage forms. Accordingly, Liang teaches that I3C and DIM improve cervical dysplasia (page 3997) and Firestone teaches the different dosage forms such as tablets, capsules, lozenges, troches, hard candies, powders, sprays, creams, suppositories, etc. (col. 14, lines 1-8). Accordingly, it would have been obvious to one of ordinary skills in the art at the time the invention was made to advance Liang's treatment that improves cervical dysplasia by adding more dosage forms to administer DIM locally as well as generally to enhance the effect of the dietary supplement to patients according to their needs.

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Applicant finally argues that Kunz does not remedy the deficiencies of Liang and/or Firestone. Applicant submits that Kunz does not teach, suggest or provide a motivation for using DIM to treat cervical dysplasia.

To respond to the above argument, Kunz administered diindoloalkaloids for treatment of a medical condition in the form of particles, this gives a motivation to administer DIM for cervical dysplasia in the form of microparticles to be able to increase the routes of administration because microparticles are easy to include in different kinds of dosage forms and are easily absorbed through different routes.

### ***Conclusion***

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

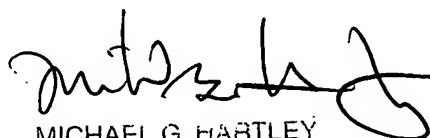
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim  
6/16/07



MICHAEL G. HARTLEY  
SUPERVISORY PATENT EXAMINER